Asthma – diagnosis and management

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Objectives

• Definition
• How to make an initial diagnosis of Asthma
• Management of Asthma
• Role of Biologics in severe Asthma.
• Role of Bronchial thermoplasty in severe Asthma
• Difference between asthma and COPD.

Asthma

Definition
• Asthma is a chronic inflammatory airway disease in which airways narrow and swell and produce extra mucus.

Pathology of Asthma

Normal airway
Asthmatic airway
Asthmatic airway during attack

Relaxed smooth muscles
Wall inflamed and thickened
Air trapped in alveoli
Tightened smooth muscles
Making the initial diagnosis

- Symptoms: Wheezing, SOB, chest tightness, cough
- Symptoms may vary overtime and in intensity
- Symptoms worse at night or early in the morning.
- Symptoms triggered by viral infections, allergens, exercise, change in weather, laughter, strong smells etc

Confirm variable airflow limitation

- Spirometry with bronchodilator challenge.
- Bronchial provocation testing.
- Positive exercise challenge test.
- Excessive variability in twice –daily peak expiratory flow over 2 weeks

Common Asthma phenotypes

- Extrinsic asthma
- Intrinsic asthma
- Late onset asthma
- Chronic obstructive asthma
- Asthma with obesity
## Classification of Asthma severity

<table>
<thead>
<tr>
<th>Frequency of symptoms</th>
<th>Severity</th>
<th>% predicted</th>
<th>Variability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day</td>
<td>Night</td>
<td>FRV/PEFR</td>
<td>PEFR%</td>
</tr>
<tr>
<td>Intermittent</td>
<td>&lt;1/wk</td>
<td>≥80%</td>
<td>&lt;20%</td>
</tr>
<tr>
<td>Mild persistent</td>
<td>≥1/wk</td>
<td>&gt;2/wk</td>
<td>≥80%</td>
</tr>
<tr>
<td>Moderate persistent</td>
<td>Daily</td>
<td>≥1/wk</td>
<td>60-80%</td>
</tr>
<tr>
<td>Severe persistent</td>
<td>Daily</td>
<td>Frequent</td>
<td>≥60%</td>
</tr>
</tbody>
</table>

Classified according to the Global Initiative for Asthma (GINA) guidelines
- Intermittent: 1 point
- Mild persistent: 2 points
- Moderate persistent: 3 points
- Severe persistent: 4 points

### Asthma Control Test (ACT)

1. In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school or at home?
   - All of the time (Score: 1)
   - Most of the time (Score: 2)
   - Some of the time (Score: 3)
   - A little of the time (Score: 4)
   - None of the time (Score: 5)

2. During the past 4 weeks, how often have you had shortness of breath?
   - More than once a day (Score: 1)
   - Once a day (Score: 2)
   - Twice or 3 times (Score: 3)
   - 4 or more a week (Score: 4)
   - Not at all (Score: 5)

3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?
   - Not at all (Score: 1)
   - Only once or twice (Score: 2)
   - Once a week or more (Score: 3)
   - Twice a week or more (Score: 4)
   - Most of the time (Score: 5)

4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as salbutamol)?
   - Not at all (Score: 1)
   - Up to 1 dose per day (Score: 2)
   - 2 or 3 doses per day (Score: 3)
   - 4 or more doses per day (Score: 4)
   - Not at all (Score: 5)

5. How would you rate your asthma control during the past 4 weeks?
   - Poorly controlled (Score: 1)
   - Sometimes controlled (Score: 2)
   - Controlled (Score: 3)
   - Mostly controlled (Score: 4)
   - Very well controlled (Score: 5)

**Patient Total Score**

### Exhaled nitric oxide

During inflammation, activated inflammatory cells demonstrate increased production of NO.

[Diagram showing the GINA cycle of asthma care]

**Diagnosis**
- Symptom control and risk factors
- Exhaled nitric oxide
- Patient satisfaction

**Therapy**
- Asthma medications
- Non-pharmacological strategies
- Treat modifiable risk factors

**Follow-up**
- Patient adherence
- Non-pharmacological strategies

**Address non-pharmacological strategies**
- Establish a partnership with the patient
- Consider health literacy, personal goals and fears, and cultural issues

**Treatment choices**
- Population-level decisions: efficacy, effectiveness, safety, cost, regulations
- Patient-level decisions: for selecting treatment, also discuss patient characteristics (phenotype that predicts response or risk), patient preference, practical issues (inhaler technique, adherence, side effects), individual risk factors

**Adjunctive care**
- Consider stepping up if uncontrolled symptoms, exacerbations or risks, but check diagnosis, inhaler technique, adherence and modifiable risk factors first
- Consider stepping down if symptoms controlled for 3 months and low risk for exacerbations

Written asthma action plan for all patients
Comorbid Contributors

- Sinusitis/Rhinitis.
- Gastroesophageal reflux disease.
- Obesity.
- Anxiety and Depression symptoms.
- Obstructive sleep apnea
- Vocal cord dysfunction

Role of Biologics in moderate to severe Asthma management

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Table 1. Summary of the Biologics Currently Approved for the Treatment of Moderate to Severe Persistent Asthma with Type 2 – High Phenotype

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Mechanism of Action</th>
<th>Indication</th>
<th>Dosing and Route</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omalizumab</td>
<td>Anti-IgE; prevents IgE from binding to its receptor on mast cells and basophils</td>
<td>≥6 yr old with moderate to severe persistent asthma, positive allergy testing, incomplete control with an ICS, and IgE: 30–1,300 IU/ml (United States, age 6–11 yr), 30–700 IU/ml (United States, age ≥12 yr), or 30–1,500 IU/ml (European Union)</td>
<td>0.016 mg/kg per IU of IgE (in a 4–wk period) administered every 2–4 wk s.c. (150–375 mg in United States; 150–600 mg in European Union)*</td>
<td>Black box warning: ∼0.1–0.2% risk of anaphylaxis in clinical trials</td>
</tr>
<tr>
<td>Mepolizumab</td>
<td>Anti–IL-5; binds to IL-5 ligand; prevents IL-5 from binding to its receptor</td>
<td>≥12 yr old with severe eosinophilic asthma unresponsive to other GINA step 4–5 therapies. Suggested AEC ≥150–300 cells/μl</td>
<td>100 mg s.c. every 4 wk</td>
<td>Rarely causes hypersensitivity reactions; can cause activation of zoster</td>
</tr>
<tr>
<td>Reslizumab</td>
<td>Anti–IL-5; binds to IL-5 ligand; prevents IL-5 from binding to its receptor</td>
<td>≥18 yr old with severe eosinophilic asthma unresponsive to other GINA step 4–5 therapies. Suggested AEC ≥400 cells/μl</td>
<td>Weight-based dosing of 3 mg/kg i.v. every 4 wk</td>
<td>Black box warning: ∼0.3% risk of anaphylaxis in clinical trials</td>
</tr>
<tr>
<td>Benralizumab</td>
<td>Anti–IL-5; binds to IL-5 receptor α; causes apoptosis of eosinophils and basophils</td>
<td>≥12 yr old with severe eosinophilic asthma unresponsive to other GINA step 4–5 therapies. Suggested AEC ≥300 cells/μl</td>
<td>30 mg s.c. every 4 wk for three doses; followed by every 8 wk subsequently</td>
<td>Rarely causes hypersensitivity reactions</td>
</tr>
<tr>
<td>Dupilumab</td>
<td>Anti–IL-4R; binds to IL-4 receptor α; blocks signaling of IL-4 and IL-13</td>
<td>≥12 yr old with severe eosinophilic asthma unresponsive to other GINA step 4–5 therapies. Suggested AEC ≥150 cells/μl and/or FeNO level ≥25 ppb</td>
<td>200 or 300 mg s.c. every 2 wk</td>
<td>Rarely causes hypersensitivity reactions; higher incidence of injection site reactions (up to 18%) and hypereosinophilia (4–14%)</td>
</tr>
</tbody>
</table>
Table 2. Efficacy of the Biologics That Are U.S. Food and Drug Administration Approved for the Treatment of Moderate to Severe Persistent Asthma with Type 2–High Phenotype

<table>
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<tr>
<th>Biologic</th>
<th>Effect on Asthma Exacerbation</th>
<th>Effect on Lung Function</th>
<th>Corticosteroid Weaning</th>
<th>Special Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omalizumab</td>
<td>Reduces by 25%</td>
<td>Minimal or equivocal</td>
<td>Decreases use of ICS</td>
<td>Only s.c. biologic approved for children 6–11 yr old</td>
</tr>
<tr>
<td>Mepolizumab</td>
<td>Reduces by ∼50%</td>
<td>Inconsistent effect</td>
<td>Decreases total use of OCS</td>
<td>Standard s.c. dosing has not been shown to decrease sputum eosinophilia; approved at higher dosing for EGPA</td>
</tr>
<tr>
<td>Reslizumab</td>
<td>Reduces by ∼50–60%</td>
<td>Improved</td>
<td>Has not been specifically evaluated for this indication</td>
<td>Only weight-based dosing</td>
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<tr>
<td>Benralizumab</td>
<td>Reduces by ∼25–60%</td>
<td>Improved</td>
<td>Decreases total use of OCS</td>
<td>Only s.c. biologic that offers every 8–wk dosing</td>
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<td>Dupilumab</td>
<td>Reduces by ∼50–70%</td>
<td>Improved</td>
<td>Decreases total use of OCS</td>
<td>Only biologic that can be self-administered s.c.; showed benefit with FeNO ≥ 25 ppb regardless of eosinophil count</td>
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Bronchial Thermoplasty in severe Asthma

- Bronchial thermoplasty (BT) is a bronchoscopic treatment for patients with severe asthma who remain symptomatic despite optimal medical therapy.
- The Global Initiative for Asthma (GINA) guidelines state that BT can be considered as a treatment option for adult asthma patients at step 5.
- BT uses temperature-controlled RF energy to impact airway remodeling, including a reduction of excessive airway smooth muscle within the airway wall.

BT reduces asthma attacks by reducing airway smooth-muscle tissue

- People who have asthma have more airway smooth-muscle tissue surrounding their airways than people who don’t have asthma. 1,2
- During an asthma attack, this excess tissue constricts the airways, making it harder to breathe. 3
- Asthma medicines help open up the airways, but these medicines don’t always work well in people who have severe asthma. 4
- BT is an add-on therapy that supplements your current asthma medications.
Is this Asthma or COPD or an overlap syndrome

COPD

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<th>Onset</th>
<th>Asthma</th>
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<td>Onset in middle life (symptoms usually begin at &gt;40 years of age)</td>
<td>Typical onset early in life</td>
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Etiology

Long smoking history or history of exposure to environmental pollutants | Possible family history of allergies or asthma |

Airflow Limitation

Not fully reversible | More reversible |

First-line maintenance treatment

Inhaled long-acting bronchodilators | Inhaled corticosteroids |

**Table 2. Bronchial Thermoplasty: Efficacy and effectiveness**

<table>
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<tr>
<th>Study</th>
<th>Patients, Follow-Up</th>
<th>Severe Exacerbations a</th>
<th>ED Visits a</th>
<th>Hospitalizations a</th>
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<td>AstraZeneca</td>
<td>76 patients, 2 years</td>
<td>4 (57%)</td>
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<td>Up to 4 (28%)</td>
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<tr>
<td>AstraZeneca</td>
<td>226 patients, 2 years</td>
<td>4 (57%)</td>
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<td>4 (48%)</td>
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Bronchial Thermoplasty

Global Registry b

| N=256, 1 year | 4 (24%) | 4 (24%) | 2 (4%) |


Usual features of asthma, COPD and ACOS

**Table 3.**

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<th>Features</th>
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<th>COPD</th>
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<td>Normal or reduced</td>
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<td>2. Respiratory Symptoms</td>
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<td>3. History of Atopy</td>
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<td>4. History of Respiratory Infections</td>
<td>Frequent upper respiratory tract infections</td>
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<td>5. Response to Treatment</td>
<td>Good response to bronchodilators</td>
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References

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• Global Strategy for Asthma Management and Prevention 2018 update
• National Asthma Education and Prevention Program (NAEPP)
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Thank you